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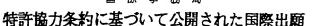
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DEX-0214

PCT

世界知的所有権機関

国際事務局





(51) 国際特許分類6 (11) 国際公開番号 A1

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PCT/JP94/01916

1994年11月11日(11.11.94)

(30) 優先権データ

特顯平5/355504

1993年11月12日(12.11.93)

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(72) 発明者

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(81) 指定国

AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN, 欧州特許(AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許(BF, BI, CF, CG, CI, CM, GA, GN, MI, MR, NE, SN, TD, TG), ARIPO特許(KE, MW, SD, SZ).

添付公開書類

国際調査報告書

補正書

(54) Title: GENE SIGNATURE

(54) 発明の名称 ジーン・シグナチャー

(57) Abstract

A 3'-directed cDNA library which accurately reflects the abundance ratio of mRNA in a cell has been prepared from various human tissues, and sequencing of the cDNAs contained in the library has been conducted to examine the incidence of each cDNA in each tissue. As each cDNA has expression information with each tissue corresponding to the mRNA concentration, these cDNAs are usable as a probe or primer for detecting cell anomaly or discriminating cells. The cloned gene can produce proteins utilizable as a medicine or the like.

Identifier:

AAN00001 DNA Sequence 134 BP

Release Info: Derwent Geneseq Database Release No. 200124; Date released 26-NOV-01

Database

XReference:

WPI; 1995-206931/27.

Accession

AAT22548

Number:

Patent Title: Identifying gene signatures in 3'-directed human cDNA library - e.g. for diagnosis of abnormal cell

function, by preparing cDNA that reflects relative abundance of corresp. mRNA in specific human tissues

Patented by: (MATS/) MATSUBARA K.;(OKUB/) OKUBO K.

Inventor:

Matsubara K, Okubo K

Description: Human gene signature HUMGS04161.

Patent ·

WO9514772-A1

Number:

Patent

Publication 01-JUN-1995

Date:

Modification

Date:

01-OCT-1996 (first entry)

Local Filing: 11-NOV-1994; 94WO-JP01916

Priority:

12-NOV-1993

Abstract:

A single-stranded DNA (or its complementary strand or the corresp. double-stranded DNA) which is comprises one of the 7837 "GS" sequences given in AAT19001-T26837 and which is able to hybridise to part of human genomic DNA, cDNA or mRNA is claimed. The GS (Gene Signature) sequences were obtained from 3'-directed cDNA libraries prepared from various human tissues; synthesis of cDNA was initiated from the 3'-end of mRNA by using poly(T) as the sole primer. Since the 3'-untranslated sequence is unique to a particular mRNA species, almost all the 3'-oriented cDNAs hybridise with specific mRNAs. Each library is constructed so as to reflect accurately the relative abundance of different mRNAs in the particular tissue from which it was derived. The appearance frequency of a given GS in a cDNA library can be determined (esp. using primers and probes derived from the GS sequences) as a means of diagnosing abnormal cell function or for recognising different cell types.

KeyWords:

Gene signature; messenger RNA; mRNA; relative abundance; frequency; human; cloning; mapping; non-

biased library; diagnosis; detection; cell typing; abnormal cell function; ss.

Organism

Homo sapiens.

Sequence Composition:

Sequence 134 BP; 32 A; 31 C; 47 G; 23 T; 1 other;

Sequence:

>AAT22548 WO9514772-A1 PA (MATS/) MATSUBARA PR 12-NOV-1993 PF 11-NOV-1994 Human

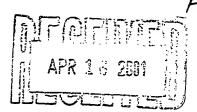
gene signature HUMGS04161. [Homo sapiens.]

GATCTGGACTGGCTGGGAGTGGGGGGGGGGGGGGGAGAGCGCTANAGGA CCCCGAGAGGGTGCAGTGGAGCCTGAGCATTGTAATATGCGGCCCAGCCTATAAACAG

CCTCCGTGCTTAAA

DEX-0115

PATENT COOPERATION TREATY



From the INTERNATIONAL SEARCHING AUTHORITY	
To:	PCT
JANE MASSEY LICATA	PCI
LICATA & TYRRELL P.C.	NOTIFICATION OF TRANSMITTAL OF
66 E. MAIN STREET	THE INTERNATIONAL SEARCH REPORT
MARLTON, NJ 08053	
Decket System	OR THE DECLARATION
Status Saport/	
State 4-bort	(PCT Rule 44.1)
WOSKEL BOOK	
6/12/07 ans	Date of Mailing
7.73	(day/month/year) 12 APR 2001
	ZN HI NEU
Applicant's or agent's file reference	
DEX-0114	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No.	International filing date
PCT/US00/31896	(day/month/year)
	21 November 2000 (21.11.2000)
Applicant	
DIADEXUS, INC.	
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1. The applicant is hereby notified that the international search	report has been established and is transmitted herewith.
Filing of amendments and statement under Article 19:	
The applicant is entitled, if he so wishes, to amend the claim	s of the international application (see Rule 46):
When? The time limit for filing such amendments is norm	nelly 2 months from the date of transmittal of the
international search report; however, for more de	
maximuomi abatot topoty no novely for more	and, out the nous on the absorbany should
Where? Directly to the International Bureau of WIPO	·
34, chemin des Colombettes	
1211 Geneva 20, Switzerland	·
Facsimile No.: (41-22) 740.14.35	·
The many data light instructions and the notes on t	sta
For more detailed instructions, see the notes on t	the accompanying sheet.
2 The applicant is hereby notified that no international search r	eport will be established and that the declaration under
Article 17(2)(a) to that effect is transmitted herewith.	
3. With regard to the protest against payment of (an) addition	al fee(s) under Rule 40.2, the applicant is notified that:
	#:
the protest together with the decision thereon has been	transmitted to the International Bureau together with the
applicant's request to forward the texts of both the pro	test and the decision thereon to the designated Offices.
no decision has been made yet on the protest; the applic	cant will be notified as soon as a decision is made.
4. Further action(s): The applicant is reminded of the following:	
Shortly after 18 months from the priority date, the international applic	
If the applicant wishes to avoid or postpone publication, a notice	
priority claim, must reach the International Bureau as provided in	. ·
completion of the technical preparations for international publicat	avii.
Within 19 months from the priority date, a demand for international	preliminary examination must be filed if the applicant
wishes to postpone the entry into the national phase until 30 mont	· · · · · · · · · · · · · · · · · ·
Within 20 months from the priority date, the applicant must perform	
before all designated Offices which have not been elected in the	
priority date or could not be elected because they are not bound b	y Chapter II.
*	<u> </u>
Name and mailing address of the TC A ITTC	Curha-bad officer //
Name and mailing address of the ISA/US	Authorized officer wides
Commissioner of Patents and Trademarks	There is a second of the secon
	Storbing Douglings Ph 1 1 1 1 1 1 1 1 1
Box PCT	Stephen LoRawlings, Ph.D.
Washington, D.C. 20231	
	Telephone No. (703) 308-0196

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY			
To: JANE MASSEY LICATA LICATA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053	PCT NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION		
	(PCT Rule 44.1)		
	Date of Mailing (day/month/year) 12 APR 2001		
Applicant's or agent's file reference DEX-0114	FOR FURTHER ACTION See paragraphs 1 and 4 below		
International application No. PCT/US00/31896	International filing date (day/month/year) 21 November 2000 (21.11.2000)		
Applicant DIADEXUS, INC.			
The applicant is hereby notified that the international search report has been established and is transmitted herewith. Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46): When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompany sheet. Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes			
Facsimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the second	ne accompanying sheet.		
2. The applicant is hereby notified that no international search re Article 17(2)(a) to that effect is transmitted herewith.	port will be established and that the declaration under		
3. With regard to the protest against payment of (an) additions	I fee(s) under Rule 40.2, the applicant is notified that:		
the protest together with the decision thereon has been applicant's request to forward the texts of both the prot	transmitted to the International Bureau together with the est and the decision thereon to the designated Offices.		
no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.			
4. Further action(s): The applicant is reminded of the following: Shortly after 18 months from the priority date, the international application will be published by the International Bureau.			
If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.			
Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).			
Within 20 months from the priority date, the applicant must perform before all designated Offices which have not been elected in the dipriority date or could not be elected because they are not bound by	emand or in a later election within 19 months from the		
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks	Authorized officer Bridges		
Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Stephen LoRawlings, Ph. D. Telephone No. (703) 308-0196		
Form PCT/ISA/220 (July 1998)	1 Non-Zentania National Property of the Control of		

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DEX-0114	FOR FURTHER ACTION		cation of Transmittal of International Search Report T/ISA/220) as well as, where applicable, item 5
International application No. PCT/US00/31896	International filing date (day/mo 21 November 2000 (21.11.2000	onth/year)	(Earliest) Priority Date (day/month/year) 22 November 1999 (22.11.1999)
Applicant DIADEXUS, INC.			4
This international search report has be applicant according to Article 18. A of this international search report consists	copy is being transmitted to the In		
<u> </u>	ed by a copy of each prior art doo	cument cite	d in this report.
language in which it was file	ed, unless otherwise indicated under	this item.	e basis of the international application in th
Authority (Rule 23.1(b)). b. With regard to any nucleotic			ne international application furnished to this
contained in the internation	nal application in written form.		<i>1</i> 66
filed together with the inte	ernational application in computer r	eadable for	m
furnished subsequently to	this Authority in written form.		•
furnished subsequently to	this Authority in computer readable	form.	
the statement that the subs		e listing doe	es not go beyond the disclosure in the
the statement that the info	rmation recorded in computer reads	able form is	identical to the written sequence listing ha
. Certain claims were four	id unsearchable (See Box I).		\mathcal{E}_{i}^{\prime}
. Unity of invention is lack	ting (See Box II).		<i></i>
With regard to the title,			
the text is approved as sub	omitted by the applicant.		
the text has been establish	ed by this Authority to read as follo	ows:	
With regard to the abstract,	-		
the text is approved as sub	omitted by the applicant.		· ·
the text has been establish	ed, according to Rule 38.2(b), by the		ry as it appears in Box III. The applicant reh report, submit comments to this
. The figure of the drawings to be p	oublished with the abstract is Figure	No.	
as suggested by the applic			None of the figures
because the applicant faile	ed to suggest a figure.		
	characterizes the invention.		

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/31896

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)	
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
1. Claim Nos.:	
because they relate to subject matter not required to be searched by this Authority, namely:	
, , , , , , , , , , , , , , , , , , , ,	
	·
2. Claim Nos.:	:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:)
	.,
3. Claim Nos.:	
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)	
Down Observations where duty of invention is factoring (continuation of feeling of first sheet)	
This International Searching Authority found multiple inventions in this international application, as follows: Please See Continuation Sheet	
,	
1 As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.	
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite	;
payment of any additional fee.	
3. As only some of the required additional search fees were timely paid by the applicant, this international search	
report covers only those claims for which fees were paid, specifically claims Nos.:	
4. No required additional search fees were timely paid by the applicant. Consequently, this international search reposits restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-7 and 16	ort
Remark on Protest The additional search fees were accompanied by the applicant's protest.	
No protest accompanied the payment of additional search fees.	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/31896

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 39/00, 48/00, 49/00; C07H 21/02, 21/04; C07K 14/00; C12N 15/11, 15/63; C12P 19/34; C12Q 1/68; G01N 33/53				
US CL : 424/9.1, 9.21, 84.1, 277.1; 435/6, 7.1, 91.2, 320.1; 514/44; 530/350; 536/23.1, 23.5, 24.31, 24.33				
B. FIEL	DS SEARCHED			
Minimum documentation searched (classification system followed by classification symbols) U.S.: 424/9.1, 9.21, 84.1, 277.1; 435/6, 7.1, 91.2, 320.1; 514/44; 530/350; 536/23.1, 23.5, 24.31, 24.33				
Documentati	ion searched other than minimum documentation to the	ne extent that such documents are include	d in the fields searched	
	ata base consulted during the international search (na Continuation Sheet	me of data base and, where practicable, s	search terms used)	
	UMENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where a		Relevant to claim No.	
A,P	Database GenCore on GenEmbl, Accession No. Al 'Homo sapiens cDNA FLJ20258 fis, clone COLF7		1, 2, 16	
A,P	Database GenCore on GenEmbl, Accession No. Al expression analyses of down-regulated cDNA C6-2 Homo sapiens DR3 mRNA, complete sequence, 26	A in human esophageal cancer'.	1, 2, 16	
A,P	Database CANCERLIT on STN, AN 2000409461, vaccines: the significant limitations of this approach Research. 2000, Vol. 20, pages. 2665-2676 (abstraction)	h to immunotherapy'. Anticancer	16	
A	Database CA on STN, AN 1998-0161021, GOODI: variant isoforms as cancer diagnostic markers'. Hi (bibliography only)		1-7	
		÷ .	,	
		·	(
	·	•	:	
*				
Further	documents are listed in the continuation of Box C.	See patent family annex.		
• S	pecial categories of cited documents:	"T" later document published after the inte		
	t defining the general state of the art which is not considered to be	date and not in conflict with the applic principle or theory underlying the inve	ention	
	oplication or patent published on or after the international filing date	"X" document of particular relevance; the considered novel or cannot be conside when the document is taken alone		
	which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as	"Y" document of particular relevance; the considered to involve an inventive ste	p when the document is	
	referring to an oral disclosure, use, exhibition or other means	combined with one or more other such being obvious to a person skilled in the		
	published prior to the international filing date but later than the ate claimed	"&" document member of the same patent family		
	ctual completion of the international search	Date of mailing of the international sea	arch report	
	01 (08.03.2001)) 12 APR	2001	
	ailing address of the ISA/US	Authorized officer	nadan	
	missioner of Patents and Trademarks PCT	Stephen L. Rawlings, Ph.D.	10-0-	
Was	hington, D.C. 20231	The state of the s	fam	
Facsimile No	o. (703)305-3230	Telephone No. (703) 308-0196	/)	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/31896

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-7 and 16, drawn to a diagnostic marker comprising SEQ ID NO: 1, a method of using said diagnostic marker to diagnose, monitor, and/or stage cancer in a patient, and a vaccine comprising said marker.

Group II, claim(s) 8, drawn to a method of identifying potential therapeutic agents.

Group III, claim(s) 9, drawn to an antibody.

Group IV, claim(s) 10 and 11, drawn to a method of imaging cancer in a patient.

Group V claim(s) 12 and 13, drawn to a method of treating cancer in a patient comprising administering an antibody that specifically binds Ovr107.

Group VI, claim(s) 14, in so far as the claim is drawn to a method of treating cancer in a patient comprising administering a molecule that downregulates expression of Ovr107.

Group VII, claim(s) 14, in so far as the claim is drawn to a method of treating cancer in a patient comprising administering a molecule that downregulates activity of Ovr107.

Group VIII, claim(s) 15, drawn to a method of inducing an immune response in a patient.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions are distinct, each from the other because of the following reasons:

Group I does not share a common technical feature with Groups II-VIII and PCT Rules 13.1 and 13.2 do not provide for multiple products and methods.

Continuation of B. FIELDS SEARCHED Item 3: All commercial sequence data bases (GenEmbl, Geneseq, Issued Patents, Est), Cancerlit, Medline, STN: medicine cluster

Search terms: SEQ ID NO: 1, Ovr107, ovarian cancer, gynecologic cancer, malignancy, tumor, diagnosis, treatment; immunization; vaccine; gene therapy, staging, Gene no. 403869, Clone no. 817834, DIADEXUS, INC.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be contounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

- ANSWER 3 OF 3 PASCAL COPYRIGHT 2001 INIST-CNRS. ALL RIGHTS RESERVED.
- PASCAL ΑN 1998-0161021
- Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved. CP
- TIEN Current status of CD44 variant isoforms as cancer
- diagnostic markers
 GOODISON S.; TARIN D. ΑU
- Nuffield Department of Pathology and Bacteriology University of Oxford, CS
- John Radcliffe Hospital, Oxford, United Kingdom Histopathology, (1998), 32(1), 1-6, 37 refs. SO ISSN: 0309-0167
- DT Journal
- BL Analytic
- CY United Kingdom
- LA English
- ΑV INIST-17811, 354000078763200010
- Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved. CP

- L23 ANSWER 1 OF 97 CANCERLIT
- AN 2000409461 CANCERLIT
- DN 20409461
- TI Failure of cancer vaccines: the significant limitations of this approach to immunotherapy.
- AU Bodey B; Bodey B Jr; Siegel S E; Kaiser H E
- Department of Pathology, University of Southern California, Los Angeles 91335, USA. Bodey18@aol.com
- SO ANTICANCER RESEARCH, (2000). Vol. 20, No. 4, pp. 2665-76. Journal code: 59L. ISSN: 0250-7005.
- DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
- FS MEDL; L; Priority Journals; Cancer Journals
- LA English
- OS MEDLINE 20409461
- EM 200010

in

AB Immunotherapy has always represented a very attractive fourth-modality therapeutic approach, especially in light of the many shortcomings of conventional surgery, radiation, and chemotherapies in the

management of cancer. Subsets of neoplastically transformed cells have been shown to (re-)express on their surface molecules which are not typically present on the surface of neighboring normal cells. In some instances, especially in malignant melanomas, cytotoxic T lymphocytes (CTLs) directed against such tumor associated antigens (TAAs) have been isolated. The cancer vaccine approach to therapy is based on the motion that the immune system could possibly mount a rejection strength response against the neoplastically transformed cell conglomerate. However, que to the low immunogenicity of TAAs, downregulation of MHC molecules, the lack of adequate costimulatory molecule expression, secretion of immunoinhibitory cytokines, etc., such expectations are rarely fulfilled. Various approaches have been explored ranging from the use of irradiation inactivated whole-cell vaccines derived from both autologous and allogeneic tumors (even tumor cell lines), and genetically modified versions of such cellular vaccines which aim at correcting costimulatory dysfunction or altering the in situ humoral milieu to aid immune recognition and activation. Anti-idiotype vaccines, based on cancer cell associated idiotypes, have also been explored which aim at increasing immunogenicity through in vivo generation of vigorous immune responses. Dendritic cell (DC) vaccines seek to improve the presentation of TAAs to naive T lymphocytes. Unfortunately, there is always the possibility of faulty antigen presentation which could result in tolerance induction to the antigens contained within the vaccine, and subsequent rapid tumor progression. The theoretical basis for all of these approaches is very well founded. Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans, however, have been somewhat disappointing. Although general immune activation directed against the

most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs in the context of the particular human

target antigens contained within the cancer vaccine has been documented

Teukocyte antigen (HLA) subclass and the necessary costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use. The use of cancer vaccines seems, at present, destined to remain limited to their employment

as adjuvants to both traditional therapies and in the management of minimal residual disease following surgical resection of the primary cancer mass.

o do	192	goctgaacagcactcotcotcoaccagcoccagcoccagcoccacctcoagctctgg 841		human esophageal Chung-Hua I'Hsuel 99445952
δ.	. 862	ctcggccccgctgggacaggcaccgctgggacagctgcgata-nctcaacggcttggacc	REFERENCE	(bases 1, to 18 Wang, M., Chen, B.,
a 6	901	CTCGGCCCCCTTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCAAGGGCTTGGACC CCGGGGGGGGGG	TITLE	Direct Submission Submitted (26-JUN
; 음	1487	CAGCGAGAAGAAAATCTCCCCAGATGCTCATCGTCAACGAGAACTGGAGGCGCGCC 1546	FEATURES	Cancer Institute, 100021, China Location
8 6	961	tggcccagggccgctcgggaccgagccgcagtcccagggccccgggcccggaaccgc 1020 	Bource	1. 1829 /organis /db_xref
o a	1691	<pre>agetcagcccgggctcggacgcctccgangtccgcgcctggctgcaggncaaggcttta 1 </pre>	CDS .	/map-m30 13, -13 /note-t /codon s
8 8	1001	gctccgggaccgtggacgctgggtgtgctgaccggggcgca-cttttctcgctgcaga 1139 		/product /protein /db_xref
o, d	1140	1140 aggagagatgogggggggggggggggggggggggggggg	<i>k</i>	LPSEGLLT IVNTSGGP PPYRPEFF AMPRLIRL
요 . 력	.1200	tgcagcgcttcgctgctggaggacaaagagaaagtgtcagagctggaggcagtgatggag 1259 	BASE COLINE	SVKORDVL PPRAPAPA RDRAAQSO
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à a	1320	cettegeaaagagtgaegaggeecegtggagaacggaeteeteagaeteteecaatag 1379	Best Lo	Best Local Similarity' 93. Matches 1569; Conservative
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ò	1560	618		69999999999999999999999999999999999999
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VERS	VERSION	AF282167.1 GI:9944939	395	ttcageggetgggagecgee
SOURCE	ORGANISM	numan. Homo sapiens Eukaryota; Metazoa; Chordata;	Db 514 TT	TTCAGCGGCTGGGAGCCGCC gagaaacagctacagcacgs
ŘEFE	REFERENCE AUTHORS		574	
		Mu, M.	Ov 488	

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FSGWEP PYTDPQSRAWEDPYEKQLOHEKRKROYTOATOGGGGWEVYGRGRS
LISYELQGSAPQVAVNGHRDLEPESEPQLESETAGKWYLCNYDFQARNSSEL
ALEVLDDSRKWWKYRDPAGQEGYVPYNILTPYPGPRIHHSGSPARSINSTPP
APPALARPRWDRPRWDSCDSLNGLDPSEKEKPPRGSSSTRNGRAWPRAA
GGPARARSSARARPPRSAGCRPNALAGGPWTRWYC"

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PAGQBGYVPYNILTPYPGPRLHHSQSPARSLNSTPPPP-PAPAPAPPRALARPRHDRPR
WDSCDSLNGLDPSBKEKFSOMLIVNEELQARLAQGRSGRSRAVPGPRAPEDOLSPGSD
SESWAMLQAKGFSSGTVOALGVLTGAQLFSLQREELRAVSPEEGARYYSQVIVQRSL
LEDKEKYSELBAWRQKKKEGEVBREVI
673 c 775 g 313 L
                                                                                          GTSSNADSÅSPDLGPRGPDLAVLQAEREVOILNIIVFDDVESFVSRLQKSAEAARVLEH
RERGRRSRRRAAGEGLLTLRAKPPSEAEYTDVLOKIKYAFSLLARLRGNIADPSSPEL
LHFLFOPLOMIVNTSGGPEFASSVRRPHLTSDAVALLRINVTPRENELHTSLGDSWTR
                                                                                                                                                              PGLÉLS PEEGPPYRPEFFSGWEPPYTDPOSRAWEDPVEROLQHERRRRQOSARQVAVN
GHRDLEPESEPQLESETAGKHYLCHYDFQARNSSEI,SVRQRUVLEVLDDSRKHHKVRD
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98.9%; Pred. No. 8.3e-246;
tive 0; Mismatches 13;
/protein_id="BAA91041
/db_xref="G1:7020230"
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NEDO human colls sequencing project
Unpublished (2000)
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Sugano, S., Suzukl, Y., Ota, T., Obayashi, M., Nishi, T., Isogai, T.,
Shibahara, T., Tanaka, T. and Nakamura, Y.
Direct Submission
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Butheria; Primates; Catarrhini, Hominidae, Homo.
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Homo sapiens colon mucosa cDNA to mRNA, clone_lib:ColF
clone:COLF7250.
                                                   AC0840
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Homo sapiens cDNA FLJ20258 fis, clone COLF7250.
AKOGO265
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/note="cloning vector pME18SFL3"
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human esophageal cancer Chung Hun I Hsueh I Chuan Hsueh Tsa Chih 16 (5), 325-327 (1051453 (bases 1 to 1829) Anglas, Check, B., Mu, K., Xu, X., Han, Y., Cai, Y., Wang, J., X Direct Submitted (16-J0N-2000) National Laboratory of Wolecular of Cancer Institute, CAMS, PUMC, Panjiayuan, Chacyang Qu, Bel Location/Qualifiers Location/Qualifiers Coganism - Homo sapiens - Anglas - An	ctgctgcgggacaacgtcactccacgtgaaaacgagctctggacctcgggggactcg 334
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9 cggagctgittgcacttccttttcgggcctctgcagatgattgtgaacacgtcg 214 cggagttodcgagcagtgtgcggaggcgcatctgacatcggatgcgtggcg 274 85.8%; Score 1403.4; DB 37; Length 1829; 93.4%; Pred. No. 1.1e-221; Conservative 0; Mismatches '9; Indels 102; Gaps a οχ q ò g q ç

> Homo saplens DRC3 mRNA, 1829 bp AF282167.1 GI:9944939 human. LOCUS
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Eukaryota; Metazoa; Chordata; Cranlata; Vertebrata; Euteleostomí; Mammalia; Eutherla; Prímates; Catarrhíní; Hominidae; Homo. 1 (bases 1 to 1829) Wu,K., Xu,Z., Wang,M., Xu,X., Han,Y., Cao,Y., Wang,R., Sun,Y. and Homo saplens

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AUTHORS REFERÊNCÉ

Cloning and expression analyses of down-regulated cDNA C6-2A in ₩u, Μ. TITLE,